Molecular characterization of Brazilian immortalized glioblastoma cell lines

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BACKGROUND: Glioblastomas are the most frequent and deadly brain tumors. Genomic alterations, as well as its high heterogeneity, are important features of these tumors. Despite the advances in the biology of these tumors, it is essential to develop models, such as primary tumor cell lines, that better mimic their genomic diversity and therapeutic behavior.

HYPOTHESIS: We aimed to characterize the molecular profile of two (HCB2 and HCB151) established immortalized glioblastoma cell lines.

METHODS: Glioblastoma cell lines, HCB2 and HCB151, were established from Barretos Cancer Hospital patients diagnosed with glioblastoma. The cells were cultured with DMEM+10%BFS+1%PS. molecularly characterized, using arrayCGH, next generation sequencing (Ion Torrent) and validated by Sanger sequencing, miRNA expression and CNV using the NanoString platform. The tumorigenic capacity was determined *in vivo* by the chicken chorioallantoic membrane (CAM) assay, and its response to temozolomide-based chemotherapy was done by MTS.

RESULTS: The aCGH analysis showed that the most frequent events was the gain of chromosome 7 and loss of chromosomes 10, 13 and 17p. HCB2 exhibited mutations in the *TERT* gene, while HCB151 showed mutations in the *TP53*, *PTEN*, *LZTR1* and *TERT* genes. The immortalized cultures present an unique miRNA profile. The CAM assay showed that HCB2 and HCB151 were able to form vascularized tumors, being HCB151 more aggressive than HCB2. In addition, both HCB2 (IC50>1000μM) and HCB151 (IC50=783μM) showed resistance to TMZ when compared to commercial glioblastomas cell lines (23-441μM). In conclusion, the present findings showed that the immortalized glioblastoma cell lines showed classic genomic features of glioblastomas and exhibited a similar biological behavior, suggesting that these cell lines are a good model for glioblastoma preclinical studies.